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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GALVEZ, JAMES JASON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,916	KLYSNER, STEEN	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-141* is/are pending in the application.

4a) Of the above claim(s) *95-99 & 101-132* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *69-94,100 and 133-141* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/23/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/23/01, 2/15/02, 7/19/04, 7/23/04, 12/9/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 2 in the reply filed on 10/26/2004 is acknowledged. The traversal is on the ground(s) that U.S restriction practices where incorrectly applied, where Unity of Invention should have been practiced. Applicant has also argued that if Unity of Invention practices are not applied that restriction is still improper on the basis of substantial "identity of classification". This is not found persuasive because although Unity of Invention was not originally applied to the instant application, the conclusion is the same. The inventions listed as Groups 1-9 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The special technical feature linking the Groups together is IL-5 or IL-5 analogues, which does not qualify as a special technical feature because under PCT Rule 13.2, a special technical feature, is one that defines a contribution of the inventions, considered as a whole, makes over the prior art. Since IL-5 and IL-5 analogues have been taught and are well known in the art, lack of unity exists (Seow, H. WO 97/00321 [03.01.1997], p. 3: lines 28-30 to p. 4: lines 1-2) and restriction as applied is deemed proper even though lack of unity was not initially set forth. Lack of Unity has been considered and consequently has been shown not to exist.

The argument that if Lack of Unity were not applied that restriction would still be deemed improper and all Groups should be examined together on the basis of "substantial identity of classification" was also not found persuasive. If all of the claims

were searched together this would place a serious burden on the Examiner and USPTO resources because, for example, it would entail searching methods and products that would require separate search strategies and separate search terms. Applicant is referred to the previous office action dated 8/26/2004 for a thorough explanation regarding distinctiveness of Groups 1-9.

Claims examined are the claims of group 2, claims 69-94 and 100, and new claims 133-141. Claims 95-99 and claims 101-132 are withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement filed 2/15/2002 has only partially been considered. The information disclosure in question has many entries that are not legible. Therefore, only entries that are legible have been considered. The information disclosure statement has been placed in the application file, but the information referred to therein has been partially considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

The use of the trademarks CORBOPOL (p. 37), INVITORGEN (p. 94, 95, and 106), SIGMA (p. 105 and 107), and DAKO (p. 106) have been noted in this application. Trademarks should be capitalized wherever they appear and should be accompanied by the generic terminology. Applicant is strongly encouraged to review the present application for any other trademarks.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69-94, 100, and 133-141 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered when determining if the disclosure satisfies written description requirements include disclosure of complete or partial structure, physical

and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof.

Claims 69-94, 100, and 133-141 are drawn to methods using an "IL-5 analogue wherein at least one foreign T_h epitope is introduced into the amino acid sequence". "Analogue" is broadly defined in the specification as an "IL-5 polypeptide which has been subjected to changes in its primary structure", which in no way limits what an "analogue" may encompass, besides changes in sequence. Thus, Applicant is claiming methods using a genus of polypeptides encompassing any conceivable change in primary structure without any structural or functional characteristics of a claimed "analogue". To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of polypeptides. Additionally, Applicant is claiming a genus in the recitation of "at least one foreign T_h epitope" because there are a myriad of T_h epitopes that are known, and yet to be discovered. The claimed foreign T_h epitopes also have no required structure and/or function. Therefore, a person of ordinary skill in the art cannot envision the claimed genus of T_h epitopes.

Claims 69-94, 100, and 134-141 are drawn to methods using a "subseqence". The specification describes "subsequence" as "any conservative stretch of at least 3 amino acids or, when relevant, of at least 3 nucleotides...". Although the definition is further limiting, Applicant is claiming methods using a genus of polypeptides.

Furthermore, Applicant has not described the common structural and/or functional characteristics of the claimed "subseqence". To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of polypeptides.

Claims 70-84 and 134-141 are drawn to methods using modifications including "at least one modification", "results in the provision of a fusion polypeptide", "substitution and/or deletion and/or insertion and/or addition", and "duplication of at least one IL-5 B-cell epitope and/or introduction of a hapten". The specification does not describe and/or limit claimed modifications. Furthermore, B-cell epitopes and haptens can encompass a plethora of molecules. Thus, Applicant is claiming methods using a genus of polypeptides encompassing numerous modifications without any structural or functional characteristics. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of modified polypeptides.

Claims 71-75 and 134-141 is drawn to methods using the following moieties: 1) "which effects targeting", 2) "which stimulates the immune system", and 3) "which optimizes presentation". The specification does not limit the claimed moieties and therefore Applicant is claiming methods using a molecules with a genus of moieties. Furthermore, Applicant has not described the common structural and/or functional characteristics of the claimed moieties. Since Applicant has provided no required

structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of polypeptides.

Claims 69-94, 100, and 134-141 are drawn methods using the following epitopes: "foreign T-cell epitope is promiscuous" and/or "natural promiscuous T-cell epitope". Epitopes claimed encompass numerous epitopes that Applicant has not adequately described. Furthermore, Applicant is claiming methods using a genus of epitopes with no described common structural and/or functional characteristics. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of epitopes to be introduced.

Claims 69 and 85 are drawn to methods using IL-5 with specified locations for modifications. Applicant has broadly claimed regions for claimed modifications of IL-5. However, the specification does not limit where those modifications can occur within the designated regions and there are no limitations on the kinds of modifications being claimed. Thus, Applicant is claiming methods using a genus of modified IL-5 polypeptides. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of polypeptides.

Claims 70-71, 81, and 135 are drawn to methods using "a binding partner of an APC specific surface antigen" or "at least one APC specific antigen is introduced". The specification does adequately limit what the binding partner or what the APC specific antigen may encompass. Applicant also admittedly states: "Many such specific surface antigens are known in the art" (p. 31: line 12). Applicant is claiming methods using a genus of molecules. Furthermore, the genus of molecules has no described common structural and/or functional characteristics. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of APC specific surface antigen binding partners to be introduced.

Claims 71 and 84 are drawn to a third moiety of "lipid nature". The specification does not adequately limit the third moiety. The recitation of "lipid nature" can encompass, and is not limited to, natural lipids and synthetic compounds that are non-polar in nature. Applicant is claiming a genus of molecules without any common structural and/or functional characteristics. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. Since Applicant has provided no required structures, properties, or functions, a person of ordinary skill in the art cannot envision the claimed genus of cytokines to be introduced.

Claims 69-94, 100, 133-141 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of downregulating IL-5 with

modifications to IL-5 (His-tag and tetanus toxoid), does not reasonably provide enablement for a method of downregulating IL-5 using IL-5 with unlimited modifications. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 69-94, 100, and 133-141 are drawn to "an immunogenically effective amount". "An immunogenically effective amount" is interpreted to elicit a general immune response since no specific immune response is disclosed that corresponds to "an immunogenically effective amount". Since the claimed invention is directed to a specific immune response, i.e. IL-5 downregulation by eliciting antibody production to a modified IL-5 wherein the antibodies facilitate breaking of autotolerance to IL-5, a person of ordinary skill in the art would not know how to use the invention as presently claimed. The specification fails to teach a person of ordinary skill in the art how to use the invention when a non-specific immune response is elicited. For the reason given above and the non-limiting manner in which Applicant has defined terms in the

disclosure it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, and the breadth of the claims.

Claims 69-94, 100, and 133-141 are drawn to methods using an "IL-5 analogue wherein at least one foreign T_h epitope is introduced into the amino acid sequence" and modifications including "at least one modification", "substitution and/or deletion and/or insertion and/or addition", and "duplication of at least one IL-5 B-cell epitope and/or introduction of a hapten". "Analogue" is broadly defined in the specification as an "IL-5 polypeptide which has been subjected to changes in its primary structure", which in on way limits what an "analogue" may encompass, besides changes in sequence. Likewise, foreign T_h epitopes and modifications are not limited by the specification and encompass the introduction of any epitope that stimulates T-cells and a vast number and array of modifications to IL-5. Applicant is claiming sequences deriving from IL-5 that Applicant does not possess. Furthermore, without a clear delineation of changes encompassed, Applicant cannot know if the modified IL-5 polypeptides are operable within the present invention. For example, single nucleotide polymorphisms (SNPs) have been shown to result in measurable structural/functional changes (Riley et al., Pharmacogenomics 2000, Vol 1(1): pp. 39-47). It is also well known in the art that single amino acid changes can severely affect polypeptide function. Luck et al. have reported that even conservative amino acid changes, R→K, can alter activity by as much as 90% (Molecular Endocrinology 1991, Vol. 5(12): pp. 1880-1886, esp. p. 1881, table 1). The references sited demonstrate that changes in primary structure can affect

both tertiary structure and function of polypeptides and that it is not be possible for Applicant to know if the broad claim of IL-5 polypeptides recited can used in the instant invention (e.g. will antibodies generated against modified IL-5 recognize both the modified polypeptide and the native polypeptide). For the reasons given above and the non-limiting manner in which Applicant has defined terms in the disclosure it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, the unpredictability of the art, and the breadth of the claims.

Claims 69-94, 100, and 134-1414 are drawn to methods using a "subseqence". The specification describes "subsequence" as "any conservative stretch of at least 3 amino acids or, when relevant, of at least 3 nucleotides...". Presently, the claim reads on any molecule sharing at least one amino acid with IL-5. The claims are broad and encompass every conceivable polypeptide that shares one amino acid with the over 100 amino acids contained within IL-5. Therefore, Applicant is claiming polypeptides that Applicant does have, which render the claims unsatisfactory from an enablement perspective, i.e. make and use the claimed invention. Furthermore, the certainty of every polypeptide that falls within the broad class of polypeptides claimed being operable within the framework of the instant invention is highly unlikely. For example, would Applicant expect similar result using polypeptides displaying disparate functions, such as myostatin, to be enabled for the present invention? Thus, a person of ordinary skill in the art would not be able to make and/or use the present invention

commensurate in scope due the quantity of experimentation necessary, the nature of invention, and the breadth of the claims.

Claims 69 and 85 are drawn to methods using IL-5 with specified locations of modifications. Applicant has broadly claimed regions for claimed modifications of IL-5. However the specification does not limit where those modifications can occur within the designated regions and there are no limitations on the kinds of modifications being claimed. Applicant is claiming sequences deriving from IL-5 that Applicant does not possess. Furthermore, without a clear delineation of changes encompassed, Applicant cannot know if the modified IL-5 polypeptides are operable within the present invention. For example, single nucleotide polymorphisms (SNPs) have been shown to result in measurable structural/functional changes (Riley et al., Pharmacogenomics, 2000, Vol 1(1): pp. 39-47). It is also well known in the art that single amino acid changes can severely affect polypeptide function. Luck et al. have reported that even conservative amino acid changes, R→K, can alter activity by as much as 90% (Molecular Endocrinology 1991, Vol. 5(12): pp. 1880-1886, esp. p. 1881, table 1). The references sited demonstrate that changes in primary structure can affect both tertiary structure and function of polypeptides and that it is not be possible for Applicant to know if the broad claim of IL-5 polypeptides recited can used in the instant invention (e.g. will antibodies generated against modified IL-5 in every position within the designated region recognize both the modified polypeptide and the native polypeptide). For the reasons given above and the non-limiting manner in which Applicant has defined terms in the disclosure it would not be possible to make and/or use the invention

commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, the unpredictability of the art, and the breadth of the claims.

Claims 69 and 100 are drawn to methods of "...treating and/or preventing and/or and/or ameliorating asthma or other chronic allergic reactions characterized by eosinophilia". Applicant has not adequately described what disease conditions are encompassed under "other chronic allergic reactions characterized by eosinophilia". The interpretation of disease conditions relating to "other chronic allergic reactions characterized by eosinophilia" is any pathological state that is characterized by elevated eosinophils in response to an allergen. There are numerous conditions that are characterized as displaying allergic eosinophilia, such as eosinophilic esophagitis and eosinophilic gastroenteritis (Mann et. al., Medical Hypotheses, **In Press, Corrected Proof**, Available online 14 October 2004). Since eosinophilic esophagitis and eosinophilic gastroenteritis may be characterized as having other divergent characteristics from eosinophilic asthma, Applicant does not know if the claimed inventions would have any use directed towards these conditions, which are also in part characterized by eosinophilia. Furthermore, it is unknown if the methods claimed could predictably treat, prevent, and/or ameliorate any pathological condition characterized by elevated eosinophils in response to an allergen. "Preventing" certain conditions based on some intervention is an issue and is especially difficult to establish because to do so Applicant must be able to provide some evidence that the pathological condition is predicable and that the intervention was able to prevent the pathological state, which

has not been established in the instant disclosure. For the reasons stated above, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, and the breadth of the claims.

Claims 71-75 and 134-141 is drawn to the following moieties: 1) "which effects targeting", 2) "which stimulates the immune system", and 3) "which optimizes presentation". The specification does not limit the claimed moieties. Furthermore, claims are drawn to molecules that Applicant does not possess. Without possession of claimed molecules Applicant cannot verify if they can be used within the framework of the instant invention. Therefore, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, the unpredictability of the art, and the breadth of the claims.

Claims 70-71, 81, and 135 are drawn to methods using "a binding partner of an APC specific surface antigen" or "at least one APC specific antigen". The specification does not adequately limit what the binding partner or APC specific antigen may be. Applicant is claiming molecules that Applicant does not possess and may not even be known. Therefore, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, and the breadth of the claims.

Claims 70-71, 82-83, and 137 are drawn to a methods using "cytokine". The specification does not limit the cytokines claimed. The interpretation of the claim is that

it encompasses all cytokines. However, cytokines exhibit divergent properties and may not be operable in the instant invention. For example, IL-12 is proinflammatory, while IL-4 is anti-inflammatory (Elenkov et al., Ann N Y Acad Sci. 2002 Jun, 966: pp. 290-303, esp. p. 291: paragraph 2). The inherent properties of cytokines are not identical and therefore precludes, without verification, definitively knowing whether or not certain cytokines are operable with the framework of the instant invention. Therefore, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, and the breadth of the claims.

Claims 71 and 84 are drawn to methods using a third moiety of "lipid nature". The specification does not adequately limit the third moiety. A recitation of "lipid nature" can encompass, and is not limited to, natural lipids and synthetic compounds that are non-polar in nature. The molecules encompassed in the claim may or may not be operable within the framework of the instant invention. For example, a moiety with a great deal of lipophilicity, and consequently hydrophobicity, may compartmentalize in adipocytes preventing or decreasing the availability of the polypeptide of interest. Therefore, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of adequate working examples, the nature of the invention, and the breadth of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 69-71 and 134-137 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to "substantial fraction". It is unclear what constitutes a "substantial fraction". For example, is a "substantial fraction" one amino acid or 100 amino acids?

Claims 69-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to "suitable chemical groups". It is unclear what "suitable chemical groups" constitute and what "suitable chemical groups" may be.

Claims 69-71, 74, and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to "an effective part". It is unclear what "an effective part" constitutes. Is "an effective part" made of a single amino acid, several amino acids, or some other part of a molecule, such as glycosylation?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the $_{h}$ invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 69-94, 100, and 133-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. (Mol Immunol. 1997, Vol. 34(16-17): pp. 1113-1120) in view of Steinaa et al. (PG Pub. No.: US 2004/0141958 A1, effective filing date 10/98) and Foster et al. (J Exp Med. 1996, Vol. 183(1): pp. 195-201). Dalum et al. teach that autotolerance to self-proteins can be overcome by introducing a T_h epitope(s) into self-proteins (p. 1118: paragraph 2). However, Dalum et al. do not teach the specific limitations of the claims, such as the downregulation of IL-5 specifically.

Steinaa et al. discloses a general method of vaccination directed towards self-proteins wherein the method involves using modified self-proteins, by inserting foreign T_h epitopes (Figure 1 and 2). Steinaa et al. also teach the use of tetanus toxoid epitope P2 and P30 as the foreign T_h epitope (Figure 4).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to implement the teachings of Dalum et al. and Steinaa et al., where Dalum et al. teach that tolerance to self proteins can be overcome by introducing foreign T_h epitopes into self proteins and Steinaa et al. teach a specific method whereby autotolerance is overcome. Furthermore, a person of ordinary skill in the art would have

been motivated to incorporate the teachings of Dalum et al. and Steinaa et al. because Dalum et al. teach that a feasible approach for therapies directed against pathogenic self-proteins is a viable option using this approach. In addition, Foster et al. teach that airway inflammation and eosinophilia correspond to IL-5, giving support for motivation to direct a method of vaccination to overcome autotolerance to IL-5 (p. 198: Figure 3-4). Furthermore, the expectation of successfully generating modified IL-5 polypeptides with foreign T_h epitopes, and consequently using modified IL-5 in a method to downregulate endogenous IL-5, are reasonably assured based on the vast wealth of technical and practical experience in the field of recombinant DNA technologies.

Claims 69-94, 100, and 133-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. (Mol Immunol. 1997, Vol. 34(16-17): pp. 1113-1120) in view of Mouritsen et al. (WO 95/05849, 8/94) and Foster et al. (J Exp Med. 1996, Vol. 183(1): pp. 195-201). Dalum et al. teach that autotolerance to self-proteins can be overcome by introducing a T_h epitope(s) into self-proteins (p. 1118: paragraph 2). However, Dalum et al. do not teach the specific limitations of the claims, such as the downregulation of IL-5 specifically.

Mouritsen et al. discloses a method of vaccination of self-proteins, by recombinantly introducing foreign T_h epitopes into said self-proteins, directed towards tumor necrosis factor, TNF. Mouritsen also discloses tetanus toxoid as a "T_h lymphocyte stimulating epitope" (p. 3: lines 20-28). Additionally, Mouritsen et al. disclose that the method of vaccination directed towards self proteins can be used to

treat inflammatory conditions targeting other isoforms of TNF and an interleukin (p. 8: lines 1-3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to implement the teachings of Dalum et al. and Mouritsen et al., where Dalum et al. teach that tolerance to self proteins can be overcome by introducing foreign T_h epitopes into self proteins and Mouritsen et al. teach a specific method whereby autotolerance is overcome. Furthermore, a person of ordinary skill in the art would have been motivated to incorporate the teachings of Dalum et al. and Mouritsen et al. because Dalum et al. teach that a feasible approach for therapies directed against pathogenic self-proteins is a viable option using this approach. In addition, Foster et al. teach that airway inflammation and eosinophilia correspond to IL-5, giving support for motivation to direct a method of vaccination to overcome autotolerance to IL-5 (p. 198: Figure 3-4). Furthermore, the expectation of successfully generating modified IL-5 polypeptides with foreign T_h epitopes, and consequently using modified IL-5 in a method to downregulate endogenous IL-5, are reasonably assured based on the vast wealth of technical and practical experience in the field of recombinant DNA technologies.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 69-94, 100 and 133-141 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,746,669. The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: a method of breaking autotolerance to IL-5 using modified IL-5, wherein the modification is the introduction of a foreign T_h epitope. U.S. Patent 6,746,669 claims the same invention verbatim, at times, as the present invention. For example, claim 87 of the instant application is identical to claim 15 of the issued patent, including the sequence of the SEQ ID No. claimed. Other claims encompass variations in scope that would be *prima facie* obvious to the artisan of ordinary skill.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D**. whose telephone number is **571-272-2935**. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JJG
12/3/2004

JANET ANDRES
PRIMARY EXAMINER